REMARKS

The specification has been amended to insert a reference to sequence identifiers for SEQ ID NOs:10-11. A revised Sequence Listing in computer readable and paper form is submitted herewith.

Claims 6, 13, and 28 have been cancelled without prejudice or disclaimer. Claims 1, 5, 7-9, 11, 12, 14-15, 17-18, 22 and 30-31 are amended. Support for the claim amendments can be found throughout the specification at, *e.g.*, page 2, line 27 to page 4, line 13; page 10, lines 16-28; and page 16, lines 4-13.

Upon entry of the amendment, claims 1-5, 7-9, 11- 12, 14-22, and 29-31 will be pending and under consideration in this application.

No new matter has been added.

The claim amendments made herein are believed to comply with either a requirement set forth in the outstanding Final Office Action, or present the rejected claims in better form for appeal. Applicants request entry of the present amendment as it places the instant application in condition for allowance or in better form for appeal.

The claim amendments and cancellations made herein have been made solely to expedite prosecution of the instant application and should not be construed as an acquiescence to any of the Examiner's rejections.

Information Disclosure Statement

Applicants acknowledge that the Information Disclosure Statement filed on December 22, 2006 has been duly considered by the Examiner and that the references cited therein have been initialed.

Sequence Compliance

The enclosed Sequence Listing (in computer readable and paper form), along with a Verified Statement under 37 C.F.R. §1.821(f), and the above amendment is believed to satisfy the sequence listing requirements. The Sequence Listing enclosed replaces the submission filed by the Applicants on December 22, 2006. Applicants hereby state that the contents of the paper and computer readable format copies of the Sequence Listing submitted herein are identical and

contain no new matter, in accordance with the requirements of 37 C.F.R. 1.821 to 1.825. Thus, the present objection to the Sequence Listing is now obviated.

Claim Objections

At pages 9-10 of the Office Action, claim 9 was objected to for the recitation of "diffracts to 2.0 Å[;]" claim 14 was objected to for the recitation of "the the crystal[;]" and claims 18 and 31 were objected to for the recitation of "hydroxyamino carbonyl[.]"

Herein, claim 9 has been amended to recite "diffracts x-rays to 2.0 Å;" the second "the" of claim 14 has been deleted, and claims 18 and 31 have been amended to recite "hydroxyaminocarbonyl." Applicants respectfully submit that these amendments render the objections to claims 9, 14, 18, and 31 moot.

Rejections Under 35 U.S.C. § 112, Second Paragraph

At pages 4-5 of the Office Action, claims 11 and 12 were finally rejected under 35 U.S.C. §112, second paragraph as allegedly lacking antecedent basis for the recitation of TACE catalytic domain (TCD) molecules.

Claim 11 (and dependent claim 12) have been amended to depend from claim 2, which provides antecedence for the recitation of "a TACE catalytic domain." The claims have been further amended to recite "TACE catalytic domains of the TACE polypeptide." While applicants do not concede to any aspect of the Office Action's stated reasons for rejection, the aforementioned amendments render this rejection moot.

At page 5 of the Office Action, claims 5, 14, and 30 were finally rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. According to the Office Action,

> claim 5 is confusing in that it is unclear as to how the polynucleotide as recited in the claim, which appears to encode a variant of SEQ ID NO:8, simultaneously encodes amino acids 1-477 of SEQ ID NO:8...[and] claim 14 and 30 are confusing in the recitation of 'crystal has the structure coordinates according to Table 1' as it would appear that TACE polypeptide of the crystal and not the crystal itself, has the structural coordinates of Table 1.

Claim 5 was also alleged to be confusing in the recitation of "Asn542 as set forth in SEQ ID NO:8."

Claim 5 has been amended herein to recite that "the TACE polypeptide of SEQ ID NO:8 is further substituted such that amino acid residue Ser266 is changed to Ala and amino acid residue Asn452 is changed to Gln." Thus, claim 5, as amended, clarifies that the amino acid sequence of SEQ ID NO:8 has been further altered to include the aforesaid additional substitutions.

Claims 14 and 30 have herein been amended to recite that "the crystalline form of the TACE polypeptide" and "the crystal of the TACE polypeptide," respectively, has the structure coordinates according to Table 1.

While Applicants do not concede to any aspect of the Office's stated reasons for rejection, these amendments render the rejections of claims 5, 14, and 30 moot.

Rejections under 35 U.S.C. §112, First Paragraph (New Matter)

At page 6 of the Office Action, claims 15-16 and 18-21 were finally rejected under 35 U.S.C. §112, first paragraph, as allegedly containing new subject matter. According to the Office Action, "Claim 15 has been amended to recite the limitation 'wherein the crystallization buffer comprises sodium citrate'...However...the cited support fails to provide support for a generic crystallization buffer comprising sodium citrate." Thus, Applicants understand the Office's position to be that because the specification does not recite the phrase "crystallization buffer comprising sodium citrate" *in haec verba*, there is no written description for such a phrase in claim 15.

Applicants respectfully traverse this rejection.

According to the MPEP, "there is no *in haec verba* requirement," however, "newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure" (underlining added; see MPEP §2163 (B)). In this regard, it is provided in the MPEP that:

> The test for determining compliance with the written description requirement found in the first paragraph of 35 U.S.C. § 112, first paragraph, is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language" (underlining added; see *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

As described in more detail below, the present application as filed reasonably conveyed to one of ordinary skill in the art that the Applicants were in possession of a crystallization buffer that includes sodium citrate, as this was a common feature of at least three species of crystallization buffers exemplified in the specification.

More specifically, the specification describes at least three species of crystallization buffers containing sodium citrate: 0.1 M Na Citrate pH 5.4, 20% w/v PEG 4000, and 20% v/v isopropanol (Buffer "D"); 0.1 M Na Citrate pH 5.0 and 40% v/v ethanol (Buffer "B"); and 0.1 M Na Citrate pH 8.7, 20% w/v PEG 4000, and 20% v/v isopropanol (Buffer "C") (*see e.g.*, page 4, lines 3-5; page 16, lines 8-11; page 33, line 21 to page 34, line 9 of the specification). For example, at page 34, the specification states that "[s]mall crystals were obtained...with either buffer B or C. Further refinement of buffer C resulted in buffer D, which allowed for crystals suitable for X-ray data collection" (page 34, lines 1-6). The specification also points individually to Buffer D, the refined form of buffers B and C, as an example of the crystallization buffer (*see* page 4, lines 3-5). Thus, at least three different species of sodium citrate-containing buffers were exemplified in the specification, all three of which provided suitable conditions for crystallization.

The scope of the aforementioned genus of crystallization buffers encompassed by the claims does not have substantial variation in view of the claims' precise structural description, *i.e.*, all the crystallization buffer comprise sodium citrate, and reduction to practice (*i.e.*, all three sodium citrate-containing buffers represented by species B, C and D were shown to provide suitable crystallization conditions). Given the defined scope of the genus of sodium-citrate containing crystallization buffers recited by the claims, Applicants respectfully submit that the specification provides ample number of species having the common feature of including sodium citrate to show that the Applicants were in possession of the claimed genus.

This conclusion is fully supported by the MPEP when it provides that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice...or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such

> identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." ..... (MPEP § 2163(II)(A)(3)(a)(ii) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406).

Therefore, in view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the new matter rejection of claim 15.

Claim Rejection under 35 U.S.C. §112, First Paragraph (Written Description)

At pages 7-11 of the Office Action, claims 1-9, 11-22, and 28-31 were finally rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description.

While Applicants do not concede to any aspect of the Office's stated reasons for rejection, this rejection has been met by amending claims 1 and 22 (and claims dependent therefrom) to recite the space group and unit cell dimensions of the crystal. Thus, as amended, claims 1 and 22 are directed to a composition comprising a crystalline form of TACE polypeptide, or a co-crystallized TACE polypeptide and a hydroxamate-based binding partner, having a $P2_1$ space group and the unit cell dimensions specified, respectively. Furthermore, claims 6, 13, and 28 are cancelled, thereby rendering the rejection of these claims moot.

Applicants point out to the Office that claims 1 and 22, as amended herein, are almost identical in scope to hypothetical claim 1 exemplified in case 4 of the "Trilateral Project WM4 Comparative Studies in New Technologies: Report on Comparative Study on Protein 3-Dimensional (3-D) Structure Related Claims" released in November 2002 ("the Trilateral Report"). The USPTO indicated in the Trilateral Report that hypothetical claim 1 would meet the written description requirement because the crystal structure of the protein is provided in the claim by specifying the cell unit dimension. More specifically, claim 1 in case 4 of the Trilateral Report is directed to a crystalline form of a known protein P, and reads as follows: "A crystalline form of protein P having unit cell dimensions of a=4.0nm, b=7.8nm, and c=11.0nm." At pages 8 and 66 of the report, the hypothetical specification of case 4 is described as including, *inter alia*, that the inventors have newly produced a stable crystalline form of protein P and that the description gives experimental data with explanations of how to make the crystals. The

Trilateral Report, at page 67, and referring to the claim of case 4, states that "the claim complies with the written description requirement because the structure of protein P is provided."

Like the hypothetical claim 1 presented in case 4 of the Trilateral Report, claims 1 and 22, as amended herein, are directed to a crystalline form of a specific known protein (*i.e.*, TACE), which was extensively characterized in the art prior to the filing date in terms of its structure and function. Also similar to the hypothetical claim 1 presented in case 4, instant claim 1 recites the unit cell dimensions of the crystal. The present specification discloses, *inter alia*, that the inventors had newly produced a crystalline form of TACE, provided TACE sequence information, experimental data with explanations on how to make the crystals, and the three-dimensional structure of a crystalline form of the TACE polypeptide (*see* specification at, *e.g.*, page 2, lines 27-29; page 3, lines 15-20; page 31, line 13 to page 36, line 15; and Table 1). Thus, Applicants respectfully submit that for at least the reasons above, the specification amply provides written description for the crystalline form of a TACE polypeptide as presently set forth in claims 1 and 22 (and the claims dependent therefrom).

Dependent claims 2-14 and 29-32 further define the crystalline forms of claims 1 and 22, respectively, by specifying the catalytic domain, amino acid sequence, hydroxamate-based binding partner, and/or structural coordinates, among others. Thus, combined with the characterization of the crystal structure of the TACE polypeptide in terms of cell unit dimensions recited in claims 1 and 22, as amended herein, these dependent claims provide ample structural and functional features in common associated with the crystal structure of the TACE polypeptide, alone or complexed with a hydroxamate-based binding partner, to show that Applicants were in possession of the claimed genus at the time the present application was filed, and thus the claims were more than adequately described by the instant application.

The Office maintains the rejection of claims 15 and claims dependent therefrom for lack of written description for allegedly failing to disclose "any other representative species of the genus of TACE proteins, TACE binding partners, and crystallization buffers and conditions that can be used to achieve a crystal of TACE polypeptide."

This aspect of the rejection has been met, in part, and is traversed, in part. Instant claim 15 is drawn to a method for crystallizing a TACE polypeptide, comprising:

(A) mixing a solution comprising:

(i) a TACE polypeptide, wherein the TACE polypeptide is the expression product of a polynucleotide encoding amino acids 1-477 of SEQ ID NO:8; and

(ii) a hydroxamate-based binding partner,

with a crystallization buffer, wherein the crystallization buffer comprises sodium citrate; and

(B) crystallizing the mixture of step (A) by drop vapor diffusion to form a crystalline precipitate.

While Applicants do not concede that any of the claims fail to comply with the written description requirement, claim 15 has herein been amended to specify that the TACE polypeptide is the expression product of a polynucleotide encoding amino acids 1-477 of SEQ ID NO:8. Claim 32 is directed to a method of crystallizing a TACE polypeptide having the particular sequence specified in the presence of a hydroxamate-based binding partner. The precise structural definition of the TACE polypeptide as claimed (including the specified amino acid residues of TACE as set forth in SEQ ID NO:8) allows the skilled artisan to readily envision the claimed invention and understand that Applicants were in possession of the claimed invention at the time of filing. The genus of TACE polypeptides encompassed by these claims does not have substantial variation, since all must encode a polypeptide having an amino acid sequence encoded by the sequences specified. The TACE polypeptide disclosed in the specification is representative of the claimed genus because: all members of the genus encode a polypeptide similar to a reference sequence; and the specification describes a method for crystallizing such a polypeptide encompassed by the claim having the specified structure (e.g., see page 31, line 13 to page 36, line 15). In light of this disclosure, the skilled artisan would have concluded, at the time of filing of the present application, that Applicants were in possession of the necessary common attributes of the members of the genus.

The instant claim has also been amended to specify that the binding partner is a "hydroxamate-based binding partner." The precise structural definition of the hydroxamate-based binding partner claimed allows the skilled artisan to readily envision the genus of claimed hydroxamate-based binding partners and understand that applicant invented what is claimed. The specification provides an example of such a hydroxamate-based binding partner: N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3 -amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide.

Applicants' arguments in support of the written description for a genus of crystallization buffers comprising sodium citrate is set forth *supra*, the substance of which is reiterated here.

As discussed above, the scope of the aforementioned genus encompassed by the claims does not have substantial variation in view of the claims' precise structural descriptions. Given the defined scope of the genus, Applicants respectfully submit that the specification provides ample number of species having a common attribute to show that the applicants were in possession of the claimed genus. In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the written description rejections under 35 U.S.C. §112.

Claim Rejection under 35 U.S.C. §112, First Paragraph (Enablement)

At pages 11-17 of the Office Action, claims 1-9 and 11-22 were finally rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. According to the Office Action,

Applicants respectfully disagree with this characterization and provide the following remarks. Claims 6 and 13 have been cancelled thereby rendering the aspect of the rejection as applied to these claims moot.

Applicants do not concede that the claims are not enabled. The Trilateral Report states that claims to a crystalline form of a polypeptide (*e.g.*, like exemplary claim 1 of case 4) satisfy the enablement requirement, if the specification teaches how to make the claimed crystals, and if one skilled in the art could use the claimed polypeptide crystal without undue experimentation (see the Trilateral Report at page 67 and case 4 of the Trilateral Report at page 66). The instant specification discloses how to make the claimed composition, *e.g.*, at pages 33-34, and one of skill in the art could have used the claimed crystal without undue experimentation. In view of the disclosure in the specification, claim 1 (and claims dependent therefrom) and claim 22 satisfy the enablement requirement. Each of the grounds raised by the Office in maintaining the position that the claims are not enabled is discussed in more detail below.

At page 13, the Office Action states that the "broad scope of the claimed crystals and crystallization methods is not commensurate with the enablement provided by the disclosure." In support of the Office's position, the Examiner states that the specification only provides a single working example of a crystal and method for making, and the specification fails to provide

guidance for other polypeptides as encompassed by the claims with an expectation of obtaining diffraction-quality crystals.

This aspect of the rejection has been met by the claim amendments made herein. As amended, instant claim 1 (and claims depending from claim 1) and claim 22 are directed to compositions comprising a polypeptide in crystalline form, wherein the polypeptide is a TACE polypeptide, and wherein the crystal is of monoclinic space group $P2_1$ and has unit cell dimensions a=61.38 Å, b=126.27 Å, c=81.27 Å, and β=107.41°. As amended, claim 15 (and the claims depending from claim 15) is directed to a method for crystallizing a TACE polypeptide comprising, *inter alia*, mixing a solution comprising: (i) a TACE polypeptide that is the expression product of a polynucleotide encoding amino acid residues 1-477 of TACE as depicted in SEQ ID NO:8; and (ii) a hydroxamate-based binding partner with a crystallization buffer, wherein the crystallization buffer comprises sodium citrate. The breadth of the claims, as amended herein, are commensurate in scope with the teachings in the specification, as described in more detail below.

Applicants' disclosure describes how to make a composition comprising a crystalline TACE polypeptide comprising the amino acid residues of TACE as depicted in SEQ ID NO:8. The amino acid sequence and domain characterization of TACE were known in the art at the time the instant application was filed and are described in the instant application. For example, a detailed characterization of the location of, and interactions between, residues and domains of TACE, and how these correlate with biological activity is provided, *e.g.*, starting in paragraphs 67 through 80 of the instant application. The location of the active site of TACE was also disclosed in the application (see paragraph 71 and FIG. 2a of the application). Moreover, the structural coordinates of human TACE were identified as set forth in Table 1 of the application.

As a result of the present invention, the TACE catalytic domain was shown to fold in a relatively stable conformation containing at least three intermolecular disulfide bonds. Applicants discovered that, unlike proteins containing flexible regions, the TACE polypeptide (and more particularly, the TACE catalytic domain described in the instant application) folded into a relatively compact structure that was capable of packing productively in the crystal lattice and forming good lattice contacts. It was known in the art, at the time the instant application was filed, that variants of proteins with known crystallization parameters were likely to readily

crystallize with similar crystal structures as long the variations introduced did not markedly affect intermolecular crystal contacts or amino acid residues important for protein stability (*i.e.*, within the hydrophobic core). *See* Itoh, S. I. and M. A. Navia (1995) *Protein Science*, (4), 2261-2268 (copy submitted herewith as Appendix A). Even mutations that had an effect in altering protein stability were found to crystallize with similar crystallization parameters as the native protein, emphasizing that well-folded proteins can exhibit crystallization properties similar to the non-mutated counterparts. *See* Sauer, U. H., S. Dao-Pin, and B. W. Matthews (1992) *Journal of Biological Chemistry* (267) 2393-2399 (copy submitted herewith as Appendix B). Therefore, in view of the stability of the TACE catalytic domain and the teachings in the specification, one of ordinary skilled in the art would have been able to practice the claimed invention, as amended herein, without undue experimentation.

With respect to the state-of-the-art in generating TACE protein variants, techniques for generating mutant TACE proteins were well known in the art and were performed routinely by molecular biologists at the time the present application was filed. The disclosure also describes and demonstrates methods for successfully crystallizing a TACE polypeptide using not one, but three crystallization buffers that comprise sodium citrate (*see* Example 2, paragraphs 100-108). Once the crystallization conditions are established, one of ordinary skill in the art could have practiced the claimed invention by routine experimentation by following the teachings provided in the specification. Two-dimensional and three dimensional structural information of the TACE polypeptide in crystal form is extensively provided throughout the application (*see e.g.*, Table 1).

Similarly, high resolution solution structure and molecular modeling techniques are extensively described in the instant application, and were known in the art at the time the application was filed. Software systems for generating three-dimensional models were also described in the specification, and were known in the art. Therefore, Applicants submit that following the teachings of the specification, one of ordinary skill in the art would have been able to generate crystals of TACE polypeptide having the structural information encompassed by the claims, following the teachings of specification by practicing routine experimentation.

The Office Action cites Branden *et al.*, Drenth *et al.*, and Kierzek *et al.* in support of the allegation that the state of the art for making a protein crystal at the time of the invention was filed was highly unpredictable.

As to the unpredictability of the crystallography art raised by the Examiner, it is acknowledged that establishing adequate protein crystallization conditions is a tedious and time-consuming process. However, this does not mandate a conclusion that the experimentation required for such process is necessarily undue as set forth by the enablement standard set out by the C.A.F.C. in *Wands*, 858 F.2d 731. The Branden reference cited by the Office describes the availability of automated methods for speeding up "the tedious work of reproducibly setting up large numbers of crystallization experiments." *See e.g.*, Branden at page 375. Methods of producing pure and homogeneous protein samples successful for crystallization can be readily obtained using recombinant techniques. *Id.*

Similarly, Kierzek *et al.* (*Biophys Chem* 91:1-20) provides that "each protein crystallizes under a unique set of conditions that cannot be predicted from easily measurable physico-chemical properties" and that "crystallization conditions must be empirically established for each protein to be crystallized." In maintaining this rejection, the Office seems to ignore the fact that the Applicants had disclosed (and optimized) in the present application several crystallization conditions of the catalytic domain of the TACE polypeptide. Not only the TACE polypeptide had been successfully crystallized at the time of filing of the present application, but also the TACE three dimensional structure had been resolved. In fact, Applicants disclosed successful crystallization conditions using at least three different buffers (all three of which contain sodium citrate) and having pH's ranging from 5 to 8.7. Thus, the above-quoted passage by Kierzek *et al.* is simply not relevant to the present application as the successful crystallization of TACE had been performed and conditions for effecting the crystallization are disclosed in the instant application.

To further support the Office's position on the lack of predictability of the art, the Examiner cites Wiencek (1999) *Ann Rev Biomed Eng* 1:505-534 as teaching that "[p]rotein solubility will change dramatically as pH is altered by ~0.5 pH units... some systems are sensitive to pH changes as small as 0.1 pH units." Applicants respectfully traverse the Office's generalization of the statements in the Wiencek reference. This reference is a general review of crystallization strategies and in the above-quoted passage lists pH as one of several factors that might influence protein solubility during crystallization. The Wiencek reference does not

necessarily state that all proteins are exceptionally sensitive to pH, but that the effect of pH in protein solubility is protein-dependent. For example, the Wiencek reference provides that:

> The protein of interest will often dictate acceptable pH ranges for crystallization. Only pH values that maintain the folded structure of the protein are acceptable conditions for protein crystal growth. (*Id.* at 514).

The TACE catalytic domain provides an example of a protein that is stable in a wide range of pH values. For example, the specification discloses that TCD formed "crystalline precipitate" over a pH range of 5.0 to 8.7 (a 3.7 change in pH units) (*see e.g.*, paragraphs 103-106 of the specification), thus suggesting that the solubility of TCD is less sensitive to pH variations than other proteins, such as the ones described above in the Wiencek reference. One skilled in the art at the filing date would have recognized that proteins that form crystalline precipitates (such as the TCD), as opposed to amorphous precipitates (which are characteristic of irreversible denaturation), over a wide range of conditions is indicative of a well-folded protein that is more likely to pack productively in a crystal lattice.

At page 17, the Office Action states that "[w]hile methods of protein crystallization were known at the time of the invention, it was not routine in the art to screen all polypeptides having a substantial number of variations and modifications as encompassed by the claims..."

This aspect of the rejection has been met by the amendments to the claims made herein. As discussed above, the application teaches how to make and use crystals of TACE polypeptides, *e.g.*, polypeptides that are the expression product of the polynucleotide encoding amino acids 1-477 of TACE as depicted in SEQ ID NO:8 and crystals of TACE polypeptides of monoclinic space group P21 and with unit cell dimensions a=61.38 Å, b=126.27 Å, c=81.27 Å, and β=107.41°. In view of the disclosure of the specification and the knowledge in the field of protein crystallography, undue experimentation would not be required to make and use the subject matter covered by the claims.

The fact that some experimentation may be required does make it, *per se*, undue. As stated in the MPEP (§2164.01),

> The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l

Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

In view of the foregoing, Applicants, therefore, respectfully request reconsideration and withdrawal of the rejections of claims 1-9 and 11-22 under 35 U.S.C. § 112, first paragraph, for failure to satisfy the enablement requirement.

CONCLUSION

For the reasons set forth above, applicants submit that all grounds for rejection have been overcome and that all of the pending claims are now in condition for allowance, which action is requested.

The required fee for excess claims and a two month extension of time is being paid concurrently herewith. A Notice of Appeal and requisite fee are also submitted herewith. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 16163-039004.

Respectfully submitted,

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